

Claims

1. A method for detecting multidrug resistance or multidrug resistance potential in a test neoplastic cell, comprising:
 - a) measuring a level of triosephosphate isomerase protein in the test neoplastic cell of a given origin or cell type, and
 - b) comparing the level of triosephosphate isomerase protein in the test neoplastic cell to the level of triosephosphate isomerase in a nonresistant neoplastic cell of the same origin or cell type,wherein the test neoplastic cell is multidrug resistant or has multidrug resistance potential if the level of triosephosphate isomerase in the test neoplastic cell is greater than the level of triosephosphate isomerase in the nonresistant neoplastic cell of the same given origin or cell type.
2. The method of claim 1, wherein measuring the level of triosephosphate isomerase in the test neoplastic cell comprises contacting a cell extract with an anti-triosephosphate isomerase antibody and measuring the level of antibody bound to cellular triosephosphate isomerase.
3. The method of claim 2, wherein measuring the level of antibody bound to cellular triosephosphate isomerase is by radiolabel.
4. The method of claim 1, wherein the test neoplastic cell is selected from the group consisting of a promyleocytic leukemia cell, a T lymphoblastoid cell, a breast epithelial cell, and an ovarian cell.
5. The method of claim 1, wherein the nonresistant neoplastic cell is from a drug-sensitive cell line selected from the group consisting of HL60, NB4, CEM, HSB2 Molt4, MCF-7, MDA, SKOV-3, and 2008.
6. The method of claim 1, wherein the test neoplastic cell is selected from the group consisting of a lymphoma cell, a melanoma cell, a sarcoma cell, a leukemia cell, a

retinoblastoma cell, a hepatoma cell, a myeloma cell, a glioma cell, a mesothelioma cell, and a carcinoma cell.

7. The method of claim 1, wherein the test neoplastic cell is from a tissue selected from the group consisting of blood, bone marrow, spleen, lymph node, liver, thymus, kidney, brain, skin, gastrointestinal tract, eye, breast, prostate, and ovary.
8. A method for detecting a multidrug resistant cell in a patient comprising:
(a) administering to the patient, a triosephosphate isomerase binding agent operably linked to a detectable label; and
(b) detecting the label operably linked to the triosephosphate isomerase binding agent, wherein the triosephosphate isomerase binding agent specifically binds to triosephosphate isomerase present in a multidrug resistant cell in the patient.
9. The method of claim 8, wherein the triosephosphate isomerase binding agent is an antibody or fragment thereof.
10. The method of claim 8, wherein the triosephosphate isomerase binding agent is selected from the group consisting of 2-(N-formyl-N-hydroxy)-aminoethyl phosphonate (IPP), phosphoglycolohydroxamate (PGH) and 2-phosphoglycolate (2-PG).
11. The method of claim 8, wherein the triosephosphate isomerase binding agent is selected from the group consisting of natural ligands, synthetic small molecules, chemicals, nucleic acids, peptides, proteins, and antibodies.
12. The method of claim 8, wherein the detectable label is selected from the group consisting of fluorophores, chemical dyes, radioactive compounds, chemoluminescent compounds, magnetic compounds, paramagnetic compounds, promagnetic compounds, enzymes that yield a colored product, enzymes that yield a chemoluminescent product, and enzymes that yield a magnetic product.

13. The method of claim 8, wherein the multidrug resistant cell is a neoplastic cell.

14. The method of claim 13, wherein the neoplastic cell is selected from the group consisting of a breast cancer cell, an ovarian cancer cell, a myeloma cancer cell, a lymphoma cancer cell, a melanoma cancer cell, a sarcoma cancer cell, a leukemia cancer cell, a retinoblastoma cancer cell, a hepatoma cancer cell, a glioma cancer cell, a mesothelioma cancer cell, and a carcinoma cancer cell.

15. The method of claim 13, wherein the neoplastic cell is selected from the group consisting of a promyleocytic leukemia cell, a T lymphoblastoid cell, a breast epithelial cell, and an ovarian cell.

16. The method of claim 8, wherein the patient is a human.

17. The method of claim 18, wherein the patient is suffering from a disease or disorder caused by the presence of the multidrug resistant cell.

18. A kit for diagnosing or detecting multidrug resistance in a test neoplastic cell comprising:
a) a first probe for the detection of triosephosphate isomerase; and
b) a second probe for the detection of a multidrug resistance marker selected from the group consisting of HSC70, nucleophosmin and vimentin.

19. A kit for diagnosing or detecting multidrug resistance in a test neoplastic cell comprising:
a) a first probe for the detection of triosephosphate isomerase; and
b) a second probe for the detection of a marker selected from the group consisting of MDR1, MDR3, MRP1, MRP5, and LRP.

20. The kit of claim 18 or 19, wherein the probe for detecting triosephosphate isomerase is an anti-triosephosphate isomerase antibody.

21. The kit of claim 18 or 19, wherein the probe for detecting triosephosphate isomerase is a triosephosphate isomerase ligand selected from the group consisting of 2-(N-formyl-N-hydroxy)-aminoethyl phosphonate (IPP), phosphoglycolohydroxamate (PGH), 2-phosphoglycolate (2-PG) and inside-out vesicles (IOVs).

5

22. The kit of claim 18, wherein the second probe is selected from the group consisting of an HSC 70 antibody, a nucleophosmin antibody, and a vimentin antibody.

10 23. The kit of claim 18, wherein the second probe is selected from the group consisting of an HSC70 ligand, a nucleophosmin ligand, and a vimentin ligand.

24. The kit of claim 18 or 19, wherein the first probe detects triosephosphate isomerase present in an extract of the test neoplastic cell.

15 25. The kit of claim 18 or 19, wherein the second probe detects a marker present of the surface of the test neoplastic cell.

20 26. The kit of claim 19, wherein the second probe is selected from the group consisting of: an MDR1 antibody, an MDR3 antibody, an MRP1 antibody, an MRP3 antibody, and an LRP antibody.

25 27. A cellular triosephosphate isomerase *in situ* detection probe for the detection of cellular triosephosphate isomerase in a patient, comprising a triosephosphate isomerase binding component and a detectable label for detection *in situ*.

28. The cellular triosephosphate isomerase *in situ* detection probe of claim 27, wherein the triosephosphate isomerase binding component is an antibody.

30 29. The cellular triosephosphate isomerase *in situ* detection probe of claim 28, wherein the detectable label is Technetium.

30. A cellular triosephosphate isomerase-targeted agent for treating or preventing a multi-drug resistant neoplasm, comprising a triosephosphate isomerase binding component and a therapeutic component, wherein the triosephosphate isomerase binding component targets the therapeutic component to the multi-drug resistant neoplasm and thereby treats the multi-drug resistant neoplasm.
31. The agent of claim 30, wherein the triosephosphate isomerase binding component is an anti-triosephosphate isomerase antibody.
32. The agent of claim 30, wherein the triosephosphate isomerase binding component is selected from the group consisting of 2-(N-formyl-N-hydroxy)-aminoethyl phosphonate (IPP), phosphoglycolohydroxamate (PGH) and 2-phosphoglycolate (2-PG).
33. The agent of claim 30, wherein said triosephosphate isomerase binding component is selected from the group consisting of natural ligands, synthetic small molecules, chemicals, nucleic acids, peptides, proteins, antibodies, and triosephosphate isomerase binding fragments thereof.
34. The agent of claim 30, wherein the therapeutic component is selected from the group consisting of Actinomycin, Adriamycin, Altretamine, Asparaginase, Bleomycin, Busulfan, Capecitabine, Carboplatin, Carmustine, Chlorambucil, Cisplatin, Cladribine, Cyclophosphamide, Cytarabine, Dacarbazine, Dactinomycin, Daunorubicin, Docetaxel, Doxorubicin, Epoetin, Etoposide, Fludarabine, Fluorouracil, Gemcitabine, Hydroxyurea, Idarubicin, Ifosfamide, Imatinib, Irinotecan, Lomustine, Mechlorethamine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitoxantrone, Paclitaxel, Pentostatin, Procarbazine, Taxol, Teniposide, Topotecan, Vinblastine, Vincristine, and Vinorelbine.
35. The agent of claim 30, wherein the therapeutic component is in a liposome formulation.
36. The agent of claim 30, wherein the therapeutic component is a radioisotope.

37. The agent of claim 36, wherein the radioisotope is selected from the group consisting of ^{90}Y , ^{125}I , ^{131}I , ^{211}At , and ^{213}Bi .

38. The agent of claim 32, wherein the therapeutic component is a toxin capable of killing or
5 inducing the killing of the targeted multi-drug resistant neoplastic cell.

39. The agent of claim 38, wherein the toxin is selected from the group consisting of a
Pseudomonas exotoxin, a diphtheria toxin, a plant ricin toxin, a plant abrin toxin, a plant saporin
toxin, a plant gelonin toxin, and pokeweed antiviral protein.

10

40. A vaccine for treating or preventing a multi-drug resistant neoplasm, comprising a
triosephosphate isomerase polypeptide, or triosephosphate isomerase polypeptide subsequence
thereof, and at least one pharmaceutically acceptable vaccine component.

15 41. The vaccine of claim 40, wherein the triosephosphate isomerase polypeptide or
polypeptide subsequence is a human triosephosphate isomerase polypeptide sequence of SEQ ID
NO.: 1.

20 42. The vaccine of claim 40, wherein the triosephosphate isomerase polypeptide subsequence
is at least eight amino acids long.

43. The vaccine of claim 40, wherein the triosephosphate isomerase polypeptide subsequence
comprises a hapten.

25 44. The vaccine of claim 40, wherein the pharmaceutically acceptable vaccine component is
an adjuvant.

30 45. The vaccine of claim 44, wherein the adjuvant is selected from the group consisting of
aluminum hydroxide, aluminum phosphate, calcium phosphate, oil emulsion, a bacterial product,
whole inactivated bacteria, an endotoxins, cholesterol, a fatty acid, an aliphatic amine, a
paraffinic compound, a vegetable oil, monophosphoryl lipid A, a saponin, and squalene.

46. A method of treating or preventing a multidrug resistant neoplasm in a subject comprising administering a cellular triosephosphate isomerase-targeted therapeutic agent of any of claims 30-39.

5

47. The method of claim 46, wherein the neoplasm is selected from the group consisting of a breast cancer, an ovarian cancer, a myeloma, a lymphoma, a melanoma, a sarcoma, a leukemia, a retinoblastoma, a hepatoma, a glioma, a mesothelioma, and a carcinoma.

10 48. The method of claim 47, wherein the subject is a human patient.

49. The method of claim 48, wherein the human patient is suffering from a disease or disorder caused by the presence of the multi-drug resistant cell.

15 50. The method of claim 46, wherein the neoplasm is from a tissue selected from the group consisting of blood, bone marrow, spleen, lymph node, liver, thymus, kidney, brain, skin, gastrointestinal tract, eye, breast, prostate, and ovary.

20 51. A method of treating or preventing a multidrug resistant neoplasm in a subject comprising administering a triosephosphate isomerase vaccine of any of claims 40-45.

52. The method of claim 51, wherein the neoplasm is selected from the group consisting of a breast cancer, an ovarian cancer, a myeloma, a lymphoma, a melanoma, a sarcoma, a leukemia, a retinoblastoma, a hepatoma, a glioma, a mesothelioma, and a carcinoma.

25

53. The method of claim 52, wherein the subject is a human patient.

54. The method of claim 53, wherein the human patient is suffering from a disease or disorder caused by the presence of the multi-drug resistant cell.

30

55. The method of claim 51, wherein the neoplasm is from a tissue selected from the group consisting of blood, bone marrow, spleen, lymph node, liver, thymus, kidney, brain, skin, gastrointestinal tract, eye, breast, prostate, and ovary.

5 56. A method for detecting whether a test cell is neoplastic comprising
a) measuring a level of triosephosphate isomerase protein in the test cell of a given origin or cell type, and
b) comparing the level of triosephosphate isomerase protein in the test cell to the level of triosephosphate isomerase in a nonneoplastic cell of the same origin or cell type,
10 wherein the test cell is neoplastic if the level of triosephosphate isomerase in the test cell is greater than the level of triosephosphate isomerase in the nonneoplastic cell of the same origin or cell type.

57. A method for detecting a neoplastic cell in a patient comprising:
15 (a) administering to the patient, a triosephosphate isomerase binding agent operably linked to a detectable label; and
(b) detecting the label operably linked to the triosephosphate isomerase binding agent, wherein the triosephosphate isomerase binding agent specifically binds to triosephosphate isomerase present on a neoplastic cell in the patient.

20 58. The method of claim 57, wherein the triosephosphate isomerase binding agent is an antibody or fragment thereof.

59. The method of claim 57, wherein the triosephosphate isomerase binding agent is selected
25 from the group consisting of 2-(N-formyl-N-hydroxy)-aminoethyl phosphonate (IPP), phosphoglycolohydroxamate (PGH) and 2-phosphoglycolate (2-PG).

60. The method of claim 57, wherein the triosephosphate isomerase binding agent is selected
30 from the group consisting of natural ligands, synthetic small molecules, chemicals, nucleic acids, peptides, proteins, antibodies, and fragments thereof.

61. The method of claim 57, wherein the detectable label is selected from the group consisting of fluorophores, chemical dyes, radioactive compounds, chemoluminescent compounds, magnetic compounds, paramagnetic compounds, promagnetic compounds, enzymes
5 that yield a colored product, enzymes that yield a chemoluminescent product, and enzymes that yield a magnetic product.

62. The method of claim 57, wherein the neoplastic cell is selected from the group consisting of a breast cancer cell, an ovarian cancer cell, a myeloma cancer cell, a lymphoma cancer cell, a
10 melanoma cancer cell, a sarcoma cancer cell, a leukemia cancer cell, a retinoblastoma cancer cell, a hepatoma cancer cell, a glioma cancer cell, a mesothelioma cancer cell, and a carcinoma cancer cell.

63. The method of claim 57, wherein the neoplastic cell is selected from the group consisting
15 of a promyelocytic leukemia cell, a T lymphoblastoid cell, a breast epithelial cell, and an ovarian cell.

64. The method of claim 57, wherein the patient is a human.

20 65. The method of claim 64, wherein the patient is suffering from a disease or disorder caused by the presence of the neoplastic cell.

66. A kit for diagnosing or detecting neoplasia, comprising:

- a) a first probe for the detection of triosephosphate isomerase; and
- 25 b) a second probe for the detection of a neoplasia marker selected from the group consisting of HSC70 and vimentin.

67. The kit of claim 66, wherein the probe for detecting triosephosphate isomerase is an anti-triosephosphate isomerase antibody or binding fragment thereof.

68. The kit of claim 66, wherein the probe for detecting triosephosphate isomerase is a triosephosphate isomerase ligand selected from the group consisting of 2-(N-formyl-N-hydroxy)-aminoethyl phosphonate (IPP), phosphoglycolohydroxamate (PGH) and 2-phosphoglycolate (2-PG).

5

69. The kit of claim 66, wherein the second probe is selected from the group consisting of a HSC70 antibody, a nucleophosmin antibody and a vimentin antibody.

70. The kit of claim 66, wherein the second probe is selected from the group consisting of an HSC70 ligand, a nucleophosmin ligand and a vimentin ligand.

10

71. The kit of claim 66, wherein the second probe detects a marker present of the surface of the test cell if it is neoplastic.

72. A cellular triosephosphate isomerase-targeted agent for treating a cancerous neoplastic cell growth comprising a triosephosphate isomerase binding component and a therapeutic component, wherein the triosephosphate isomerase binding component targets the therapeutic component to the neoplastic cell growth and thereby treats the cancer.

15

73. A method of treating or preventing a neoplasm in a subject comprising administering a cellular triosephosphate isomerase-targeted therapeutic agent of claim 72.

20

74. The method of claim 73, wherein the neoplasm is selected from the group consisting of a breast cancer, an ovarian cancer, a myeloma, a lymphoma, a melanoma, a sarcoma, a leukemia, a retinoblastoma, a hepatoma, a glioma, a mesothelioma, and a carcinoma.

25

75. The method of claim 73, wherein the subject is a human patient.

76. The method of claim 75, wherein said human patient is suffering from a disease or disorder caused by the presence of the multi-drug resistant cell.

30

77. The method of claim 73, wherein the neoplasm is from a tissue selected from the group consisting of blood, bone marrow, spleen, lymph node, liver, thymus, kidney, brain, skin, gastrointestinal tract, eye, breast, prostate and ovary.